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10/537,203	06/03/2005	Andre S. Gamelin	GTI-1800-US	3433

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EXAMINER	
HOBBS, MICHAEL L	

ART UNIT	PAPER NUMBER
1797	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/537,203	GAMELIN ET AL.	
	Examiner	Art Unit	
	MICHAEL HOBBS	1797	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 January 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-47* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-47* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment filed on 01/06/2009 has been considered and entered for the record. Claims 1-47 are pending further examination upon the merits.

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 1-4, 8-15, 19, 28, 30, 40 and 41 are rejected under 35 U.S.C. 102(b) as being anticipated by Kawamura et al. (US 5,183,744).

4. Kawamura teaches a cell handling method that includes for claim 1 a plurality of wells or micro-chambers (1103) that have two electrodes within each chamber (1802, 1803) which are connected by lead wires (1011, 1012, 1020 & 1023) to a electric control unit (col. 5 lines 30-38). The voltage can be independently applied to each electrode (col. 5 lines 39-40, Figures 1, 6 & 8). For claim 2, the are at least 2 wells if not more on the device of Kawamura (Fig. 6) and the wells for claim 3 have a uniform shape of 10 μm x 10 μm (col. 4 lines 39-44). Also, for claim 4, the wells can have a rectangular shape of 10 μm x 100 μm (col. 4 lines 40-42).

5. For claim 8, the electrodes of Kawamura are on opposite sides of the well or micro-chamber (Fig. 6) where for claim 9 each micro-chamber has a sidewall and a bottom wall (Fig. 6). Furthermore, for claim 10, each chamber is individually provided

with an electrode pair for generating an electric field within the chamber and is part of the sidewall of the chamber (col. 5 lines 61-62, Fig. 6). The chambers or absorption ports are arranged in a 10 μm x 10 μm matrix which implies that the ports are in a row and column format (col. 3 lines 20-24).

6. As discussed above, the electrodes are connected to the power source individually and the power source is fully capable of providing power to each well or adsorption port simultaneously with regards to the electrodes of claim 12. Also, for claim 13, Kawamura does not specifically teach that each row can be energized independently from another row, as discussed above, each electrode can be energized individually and the electrodes of Kawamura are fully capable of having one row can be energized independently over another row. Furthermore, for claim 14, each electrode can be operated independently which includes that an electrode in one row can be energized independently over an electrode in another row (col. 5 lines 61-62). With regards to claim 15, Kawamura teaches that there are two electrodes in each well with each pair being individually energizable where a "plurality" is being interpreted to mean more than one.

7. With regards to claims 19 and 29, Kawamura discloses that a voltage can be independently applied to each electrode (col. 5 lines 39-40, Figures 1, 6 & 8) which are connected to the power source by lead wires (col. 5 lines 91-64). With regards to claim 30, Kawamura teaches the plate as described above for claim 1 and that a power supply is connected to the plate (col. 5 lines 64-66). For claim 20, Kawamura teaches that the substrate can be made from ceramics (col. 10 lines 23-26) and a ceramic

substrate would be opaque to light which reads on the limitation of claim 23. With regards to claim 24, Fig. 6 of Kawamura shows that the electrodes are integrated within the well.

8. For claim 40, Kawamura discloses the steps of providing an electric field across the membranes of a cell that are suspended in a gene suspended liquid. The electric voltage opens up micro-holes within the cell membranes which allows the genes to be injected within the cells (col. 12 lines 54-59). For claim 41, the gene injected into the cell is being interpreted as a nucleic acid since a "gene" is a portion of a DNA chain.

9. Therefore Kawamura meets the limitations of claims 1-4, 8-15, 19, 28, 30, 40 and 41.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

12. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

13. Claims 5-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kawamura et al. (US 5,183,744) in view of Nova et al. (US 6,284,459 B1).

14. Kawamura is silent regarding the specific volume of the wells.

15. Nova teaches a solid support matrix that includes a plurality of wells which are in contact with a recording device. Nova teaches for claims 5-6 a number of wells or vials for a micro-titer plate that have a volume from about 1 ml to 1.5 ml or less (col. 12 lines 30-37) which anticipates the volume ranges of 1 μl to 10 ml, 1 μl to 1 ml and 1 ml to 10 ml. The overall volume of the sample tested within the plate determines the number of wells and volume that will be tested. Typical total volumes for micro-titer or electroporation plates run on the scale of 100 ml or less to about 10 ml or less. Modifying a plate to include larger or smaller amounts of samples is within the skills of one of ordinary skill in the art. Therefore, it would be obvious to one of ordinary skill in the art to employ the well sizes as suggested by Nova in order to increase or decrease the amount of samples tested within Kawamura. The suggestion for doing so at the

time would have been in order to increase the throughput of testing and provide a convenient plate size for optical testing.

16. Claims 16-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kawamura et al. (US 5,183,744).

17. However, for claim 16, Kawamura does not teach that there are between 2 and 12 pairs of electrodes within each well. The use of multiple electrodes within each well would allow the electric field to be uniform across the entire volume of the well. Further, the addition of more than one set of electrodes within the well would be within the skills of one of ordinary skill in the art. Therefore, it would be obvious to place a multiple electrodes within the well of Kawamura in order to have a uniform electric field across the cell. See MPEP § 2144.04 VI B.

18. For claim 17, Kawamura does not specify that one electrode is a cathode and another is an anode. In order to provide an electric field across the well, it would be an intrinsic property of the electrodes that one would be a cathode and the other would be the anode in order to generate an electric field within the well. Also, for claim 18, the electrodes of Kawamura are fully capable of being energized at the same time.

19. Claims 21and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kawamura et al. (US 5,183,744) in view of Zou et al. (US 2003/0008286 A1).

20. Kawamura teaches a substrate made from ceramics which is being interpreted as being opaque and not transparent or translucent. Zou teaches a miniaturized

thermal-cycler that is used for an array of micro-chemical reactions with each proceeding at a different temperature. The substrate of Zou is made of a plastic such as polypropylene or polycarbonate (page 1 [0004]) which can be transparent as in claim 21 or translucent as in claim 22. The use of a transparent or translucent substrate allows for optical testing of the reaction chamber without having to include an optical window as part of the manufacturing process. Further, a transparent or translucent plastic substrate would be less expensive to manufacture than either a metal or glass substrate. Therefore, it would be obvious to one of ordinary skill in the art to employ the plastic substrate as suggested by Zou in order to have a chip that can be optically monitored within the teachings of Kawamura. The suggestion for doing so at the time would have been to develop and manufacture an inexpensive thermal-cycler that is also disposable (page 1 [0002]).

21. Claims 25-27 and 42-46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kawamura et al. (US 5,183,744) in view of Baer (US 5,128,257).

22. Kawamura is silent about depositing the electrode on the surface of the chip.

23. Baer teaches an elctroporation apparatus that allows cells to adhere to a surface and where two distinct electrical impulses are used to transfer a substance into the cells. With regards to claims 25-27, Baer teaches that the electrodes are deposited onto the substrate by vapor deposition (Fig. 13). Specifically a copper vapor or a metallic vapor such as aluminum or gold may be deposited on a flat planar surface such as mica or polystyrene (col. 8 lines 61-66). The use of vapor deposition is known within

the art for depositing electrodes on to a surface. Other uses for this technique include the construction of strain gauges or thermocouples for applications such as monitoring the strain or temperature of a turbine blade. Therefore, it would be obvious to one of ordinary skill in the art to employ the vapor deposition of Baer to place the electrodes within the wells of Kawamura. The suggestion for doing so at the time would be in order to from multiple directionally distinct electrodes (col. 9 lines 3-5).

24. For claim 29, as stated above, Kawamura includes independent connections for the electrodes that allow each electrode to be energized independent of the other electrodes.

25. With regards to claims 42-45, Baer teaches using mouse L-cells (col. 4 lines 2-5) which are eukaryotic (have a nucleus), animal (a mouse) and are mammalian cells. By using mouse cells, this reads on the cells being murine (rodent). Furthermore, for claim 46, a mammalian cell line such as a Chinese hamster ovary (CHO) cell line is used within the device (col. 12 lines 3-4) which implies that the mouse cells also come from an established line. The use of these types of cells for electroporation is known within the art and would be obvious to one of ordinary skill to employ the cells of Baer in order to receive the gene from the solution of Kawamura. The suggestion for doing so at the time would have been to use the type of cell that meets the fiscal and regulatory (Federal and local) constraints of the testing regime.

26. Claims 28 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kawamura et al. (US 5,183,744) in view of Baer (US 5,128,257) in further view of Malin et al. (US 5,643,742).

27. Both Kawamura and Baer are silent regarding the use of a pin and socket electrical connection.

28. Malin dicloses a system for electronically monitoring and recording cell cultures. For claim 28, Malin teaches that the electrical connection within the well consists of a pin within a socket (28). The electrical connection for the electrodes with the exterior power source is facilitated by a trace (24) or pin connection with a circuit board (col. 4 lines 24-30). Furthermore, a pin and socket electrical connections are used for connecting circuit boards with specific pieces of hardware within in a computer, i.e. hard drive, power source, cooling fans and is known to provide secure connections between two devices. Therefore, it would be obvious to one of ordinary skill in the art to employ the pin and socket circuit board connection as suggested by Malin in order to connect the electrodes with the external power source of Kawamura and Baer. The suggestion for doing so at the time would have been in order to provide a reliable electrical connection between the electrodes and the power source (col. 3 lines 2-5).

29. Claims 31-36, 38 and 39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kawamura et al. (US 5,183,744) in view of Kapur et al. (US 6,548,263 B1).

30. Kawamura is silent regarding a plate handler or plate reader.

31. Kapur discloses a miniaturized cell array for screening differentiated stem cells. For claim 31, Kapur teaches a stage (64) or plate handler that is configured to hold the plate containing the micro-wells and for claim 32 optical analysis of the sample is conducted by a luminescence reader instrument (44) (col. 22 lines 23-27). For claim 33, the optical system of Kapur is an optical spectroscopic system the uses a monochromatic light and a CCD array (82) to read the entire well array (col. 37 lines 16-20). For claim 34, the plate reader is integrated with the plate handler system for obtaining an optical result from the wells of the plate (Fig. 13). The use of a plate holder or movable stage to manipulate the electroporation plate as suggested by Kapur would be obvious to one of ordinary skill in the art in order to obtain optical data regarding the reaction of Kawamura. The suggestion for doing so at the time would be to observe each reaction within the wells, especially if each well contains a different sample or reaction.

32. With regards to claim 35, the plates of Kapur are transferred from storage units (48,54) to the optical tester by robotic arms (50,52). For claim 36, the plates are stored in either a first or second storage areas (48,54) when not being tested. With regards to claims 38 and 39, Kapur teaches a computer (56) with a database (90) for storing data from the test (col. 57 lines 13-17). Furthermore, the computer of Kapur is fully capable of optimizing the conditions within the well. Automated, robotic systems are known solutions for storing, indexing and handling micro-well plates. Using such a system would lead to greater testing throughput and optimization of the reaction parameters, i.e. temperature, humidity, etc.... Therefore, it would be obvious to one of ordinary skill

in the art to employ the robotic system and computer of Kapur in order to remotely test and optimize the reaction of Kawamura. The suggestion for doing so at the time would have been in order to minimize operator error during processing of the samples within the elecroporation plate.

33. Claim 37 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kawamura et al. (US 5,183,744) in view of Kapur et al. (US 6,548,263 B1) and in further view of Giuliano et al. (US 6,416,959 B1).r

35. Both Kawamura and Kapur are silent regarding an incubator to store the electroporation plate.Giuliano teaches a cell based screening system for introducing a purified protein into a cell. Giulian teaches that cell samples such as T3 cells were placed within the wells and incubated for 24-30 hours (col. 26 lines 42-45). Luminescent probes used for optical testing can be inserted within the cells by mechanical means such as electroporation (col. 15 lines 25-29). The use of an incubator for storing and cultivating cells with an electroporation process is within the skills of one of ordinary skill in the art. Further, it would be obvious to one of ordinary skill in the art to employ an the incubator suggested by Giuliano in order to stabilize and cultivate the cells within the teachings of Kawamura and Kapu

37. Claim 47 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kawamura et al. (US 5,183,744) in view of Giuliano et al. (US 6,416,959 B1) and in further view of Murry et al. (US 5,371,003).

38. Kawamura is silent regarding a eukaryotic cell that is a plant cell. Giuliano teaches that a plant cell can be used for introducing DNA, but is silent regarding the plant cell being a monocotyledonous plant or a dicotyledonous plant. Murry teaches an electro-transformation process that introduces DNA into a plant cell utilizing an electric current. With regards to claim 47, Murry teaches introducing naked RNA into whole cells of dicotyledonous plants (dicots) by electroporation (col. 1 lines 64-66, Abstract). Electroportation for the insertion of DNA or RNA into a plant or animal cell was a known method at the time of the invention. Whether a monocot or a dicot was used depended on the type of plant being cultivated, i.e. maize. Therefore, one of ordinary skill in the art would find it obvious to use a dicotyledonous plant as suggested by Murry in order to introduce genetic material into the cells of Kawamura and Giuliano. The suggestion for using a dicot at the time of the invention would have been to increase the survival rates of the cells that had been injected with a genetic material such as DNA (col. 2 lines 4-6).

Response to Arguments

40. Applicant's arguments filed 01/06/2009 have been fully considered but they are not persuasive. Applicant argues on page 2 paragraph 2 that he micro-chamber of US 5,183,744 is not the equivalent of the well of the instant application. The Examiner respectfully disagrees since the micro-chambers do have a bottom, a sidewall and the top of the micro-chamber is open as shown in Figure 6. Furthermore, in response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., that the well has

a closed, solid bottom wall) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Conclusion

41. Claims 1-47 are rejected.

42. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MICHAEL HOBBS whose telephone number is (571)270-3724. The examiner can normally be reached on Monday-Thursday 7:30 AM - 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill Warden can be reached on (571) 272-1267. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/William H. Beisner/
Primary Examiner, Art Unit 1797

/M. H./
Examiner, Art Unit 1797